REMARKS/ARGUMENTS

The Pending Claims

Claims 1-3, 6-19, 21, and 42-58 are pending. Claims 2, 3, 11, 12, and 42-58 are withdrawn as being drawn to a non-elected invention in response to a restriction requirement. Thus, claims 1, 6, 10, 13-19, and 21 currently are under examination.

The Office Action

Claims 1, 6-10, 13-19, and 21 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Gu et al., *Vaccine*, *17*: 340-344 (1999) ("the Gu reference"), Wu et al., *Proc. Natl. Acad. Sci. USA*, *92*: 11671-11674 (1995) ("the Wu reference"), Farina et al., *J. Virol.*, *75*: 11603-11613 (2001) ("the Farina reference"), Mogridge et al., *J. Bacteriol.*, *183*: 2111-2116 (2001) ("the Mogridge reference"), and Hamdan et al., *Parasitol Res.*, *88*: 583-586 (2002) ("the Hamdan reference"). Reconsideration of this rejection is respectfully requested.

Discussion of Obviousness Rejection

Claims 1, 6-10, 13-19, and 21 allegedly are obvious under Section 103 over the combined disclosures of the Gu, Wu, Farina, Mogridge, and Hamdan references. This rejection is traversed for the reasons set forth below.

The Gu reference allegedly discloses a DNA plasmid vaccine encoding an immunogenic portion of *B. anthracis* protective antigen (PA). The Wu reference allegedly discloses a viral vector encoding the LAMP-1 signal peptide, the HPV16 E7 gene sequence, and the LAMP-1 sorting signal for use as a vaccine. Gene expression from the viral vector allegedly resulted in enhanced MHC II presentation of the E7 protein on antigen presenting cells (APC). The Wu reference also allegedly discloses that using a LAMP-1 sequence improves vaccine potency.

The Farina reference allegedly discloses a replication-defective vector based on a chimpanzee adenovirus which can be used as a vaccine construct. The Mogridge reference allegedly discloses a nucleic acid sequence encoding a mutated form of *B. anthracis* PA which exhibits impaired oligomerization ability. The Hamdan reference allegedly discloses a

method of redesigning *S. manosoni* cDNA using recursive PCR and human-preferred codons. The Hamdan reference also allegedly suggests that codon optimization is a valuable method for improving heterologous expression of bacterial genes in human cells.

According to the Office, it would have been obvious to one of ordinary skill in the art to modify the PA-encoding plasmid vaccine (as disclosed by the Gu reference) and employ a LAMP-1 sorting signal (as disclosed by the Wu reference) and a viral vector (as disclosed by the Wu and Farina references) using known recombinant DNA methodology to "predictably yield" the claimed gene transfer vector. The Office acknowledges that SEQ ID NO: 1 is not disclosed in the prior art. Nevertheless, the Office states that the Mogridge and Hamdan references disclose the process of codon optimization, specifically codon optimization of the PA gene, to improve the expression of an antigen in a mammalian cell. The Office contends that the the invention defined by the pending claims is obvious because the cited references provide "a finite number of predictable codon optimized PA sequences, sorting signals, and viral vectors with a reasonable expectation of success" (Office Action, pages 6-7, bridging paragraph).

Contrary to the allegations of the Office, the cited references do not describe a finite number of predictable codon optimized PA sequences. Specifically, the native PA sequence contains 765 codons. Thus, each of the 765 codons could be modified, separately and in various combinations, to be human-preferred codons. As such, there are thousands of possible ways that the native PA sequence could be modified via codon-optimization. Thus, it cannot be reasonably asserted that the cited prior art references, alone or in combination, disclose a "finite number" of predictable codon optimized PA sequences for one of ordinary skill in the art to systematically test, much less choose SEQ ID NO: 1.

Based on the foregoing, Applicants submit that the cited references do not provide any teaching of, or pointer to, the gene transfer vector of claim 1, particularly due to the countless number of possible codon-optimized PA sequences. As a result, one of ordinary skill in the art would not have found it "obvious to try" various codon-optimized PA sequences so as to arrive at a gene transfer vector comprising SEQ ID NO: 1. To assert otherwise, relies on improper and impermissible hindsight knowledge of Applicants' invention.

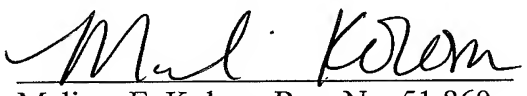
In considering whether or not the present invention is unobvious over the combination of the cited references, the Office must avoid the improper use of hindsight reconstruction, namely utilizing the pending claims as a template for selecting particular portions of particular references to combine in such a way so as to yield the present invention without any consideration of what one of ordinary skill in the art at the relevant time actually would have faced in seeking to solve the problem at hand. As stated by the Federal Circuit: "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit." *Grain Processing Corp. v. American Maize-Products Corp.*, 840 F.2d 902, 5 U.S.P.Q.2d 1788 (Fed. Cir. 1988).

Based on the foregoing, Applicants submit that the obviousness rejection is without merit and should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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